Lasers in Surgery and Medicine 22:228–239 (1998)

Acute Results, Complications, and Effect of Lesion Characteristics on Outcome With the Solid-State, Pulsed-Wave, Mid-Infrared Laser Angioplasty System: Final Multicenter Registry Report

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Background and Objective: **The solid-state, mid-infrared holmium:YAG laser (2.1 μm wavelength) is a relatively new percutaneous device that has recently been evaluated in a multicenter study. Because of its unique wavelength and photoacoustic effects on atherosclerotic plaques, this laser may be useful in treatment of symptomatic patients with coronary artery disease. This study sought to evaluate the safety and efficacy of mid-infrared laser angioplasty in the treatment of coronary artery lesions.**

Patients and Methods: **Laser angioplasty was performed on 2,038 atherosclerotic lesions in 1,862 consecutive patients with a mean age of 61 ± 11 years. Clinical indications included unstable angina (69%), stable angina (20%), acute infarction (6%), and positive exercise test (5%). Complex lesion morphology included eccentricity (62%), thrombus (30%), total occlusion (27%), long lesions (14%), and saphenous vein grafts (11%).**

Results: **This laser catheter alone successfully reduced stenosis (>20%) in 87% of lesions. With adjunct balloon angioplasty, 93% procedural success was achieved. The presence of thrombus within the target lesion was a predictor of procedural success (OR = 2.0 [95% confidence interval 2.0, 4.0], *P* = .04). Bifurcation lesions (OR = 0.5 [95% confidence interval 0.2, 1.0], *P* = .05) and severe tortuosity of the treated vessel (OR = 0.4 [95% confidence interval 0.2, 0.9], *P* = .02) were identified as significant predictors of decreased laser success. Calcium within the lesion was associated with reduced procedural success (OR = 0.57 [95% confidence interval 0.34, 0.97], *P* = .03), and calcified lesions required significantly more energy pulses than noncalcified lesions (119 ± 91 pulses vs. 101 ± 86 pulses, respectively, *P* = .0002). Complications included in-hospital bypass surgery 2.5%, Q-wave myocardial infarction 1.2%, and death 0.8%. Perforation**

Contract grant sponsor: Scimed.

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Accepted 31 December 1997

occurred in 2.2% of patients; major dissection in 5.8% of patients, and spasm in 12% of patients. No predictor of major complications was identified. Six-month angiographic restenosis was documented in 54% of patients, and clinical restenosis occurred in 34% of patients.
Conclusion: **Mid-infrared laser has a safety profile similar to that of other debulking devices. This laser may be useful in select patients presenting with acute ischemic syndromes associated with intracoronary thrombus; however, like other coronary lasers, it is limited by the need for adjunctive balloon angioplasty and/or stenting to achieve adequate final luminal diameter. No beneficial effects on reducing 6-month restenosis rates were observed. Lasers Surg. Med. 22:228–239, 1998.**

Key words: angioplasty; arteries; coronary disease; laser; revascularization; thrombus

INTRODUCTION

Over the last decade, several alternate interventional devices have been developed for lesions considered "non-ideal" for conventional balloon angioplasty. Lasers attracted significant attention due to their unique interaction with atherosclerotic plaque which results in tissue ablation and removal, rather than displacement [1]. The ultraviolet, gaseous medium excimer laser [2,3] has recently been approved by the Food and Drug Administration. A solid-state (holmium:YAG), pulsed-wave, mid-infrared (2.1-μm wavelength) laser is an investigational, new coronary laser system under observation in a multicenter registry study. This study reports the acute results of holmium:YAG laser-assisted angioplasty, clinical and angiographic complications, effect of lesion characteristics on outcome, as well as 6-month angiographic and clinical restenosis rates in 1,862 patients enrolled in the multicenter registry.

MATERIALS AND METHODS

Patient Population

A multicenter registry assessing the feasibility and safety of a mid-infrared laser in treatment of atherosclerotic lesions in native coronary arteries and saphenous vein grafts was established in April 1990 and subsequently included 44 centers. Data collection ended in October 1995. Patients were enrolled with symptomatic coronary artery disease or following positive exercise test whose coronary angiography demonstrated lesions with >70% reduction in lumen diameter. Exclusion criteria included unprotected left main coronary artery, severe angulation (>90%), presence of coronary dissection, lesions in vessels with a diameter smaller than the laser catheter diameter, and lesions not traversable by guidewire. The protocol for this study was approved by the FDA and local IRBs, and all patients gave written, informed consent.

Laser Device

The solid-state, mid-infrared holmium:YAG device (Eclipse 2100, Eclipse Surgical Technologies, Palo Alto, CA) requires 220 volts and 20 amperes of single-phase power. Laser output is activated with a foot pedal, delivering pulses of 250 μseconds at a pulse width of 250 to 600 mJ/pulse at a frequency of 5 Hz. Laser light with a 2.09 μm wavelength is transmitted through multiple optical low-OH flexible silica fibers and emitted from the distal tip of the catheter in front-firing mode. The penetration depth in vascular tissue is 400 μm. The threshold fluence for vascular tissue ablation is 300 mJ/mm^2 per pulse. Six multifiber over-the-wire catheters are available: 1.2 mm (27 optical fibers, 75 μm each), 1.3 mm (20 optic fibers, 100 μm each), 1.4 mm (40 optic fibers, 50 μm each), 1.5 mm (26 fibers, 100 micron each), 1.7 mm (49 fibers, 50 μm each), and 2.0 mm (12 fibers, 100 μm each). The laser catheter has a central lumen that accepts 0.014″ or 0.018″ guidewires.

Laser Procedure

The laser device is turned on and placed on a standby mode, and lasing energy requirements are calculated and set according to manufacturer's guidelines. Preparation of the laser catheter entails flushing the catheter with 10 cc heparinized saline and connecting its proximal end to the laser device via a simple screw mount. Depending

on the laser catheter size, an 8-French (for 1.2-, 1.3-, 1.4-, and 1.5-mm catheters) or 9-French guiding catheter (for 1.7-mm and 2.0-mm catheters) is utilized. After engagement of the vessel ostium, a 300-cm angioplasty guidewire is passed across the lesion using a bare-wire technique, and its floppy tip positioned in the distal vessel. Device size selection matched the lesion severity, not the reference diameter of the target vessel. For lesions with ≥90% stenosis severity, 1.2-mm up to 1.4-mm catheters were used; for 80–90% stenosis 1.5-mm or 1.7-mm catheters were utilized; and for lesions of 70–80% stenosis severity a 2.0-mm catheter was applied. Once the guidewire is in position, the laser catheter is advanced upward to 2-mm from the lesion. At this time the personnel and the patient are equipped with laser protection goggles. Intracoronary nitroglycerin is administered, and the laser device is placed in a ready mode. In the early experience of the registry the traditional lasing technique [4] was applied, incorporating steady advancement of the laser catheter across the target lesion while continually emitting laser pulses. This method was replaced in most participating centers by a "pulse and retreat" lasing technique [5], in which lasing is initiated in a non-contact mode, i.e., beginning lasing emission at 1 mm before the lesion. Under fluoroscopy the catheter is then slowly advanced toward the lesion, delivering only a small number of pulses, typically 8 to 12 per session at a repetition rate of 5 pulses/second. After each lasing session the catheter is retracted into the proximal, larger portion of the artery or into the guiding catheter to permit unobstructed forward coronary flow. A pause of 45–60 seconds is taken prior to the next lasing session to allow cooling, intracoronary nitroglycerin administration, and gas bubble dissipation. A combination of tactile feedback and angiography is used in deciding how many passes through the lesion are necessary. If a catheter cannot successfully ablate at the initial energy delivery parameters selected, the fluence is increased according to appropriate ranges for a given catheter size. Repeat angiography is performed after the laser catheter is retracted to assess post-lasing results. In the vast majority of cases subsequent balloon angioplasty was performed for further reduction of lesion stenosis. Coronary stents were not used in this study. Repeat angiography is obtained for documentation of final results.

Medications

All patients were pretreated with aspirin (325 mg/day) and calcium channel blockade. After arterial access was obtained, heparin 10,000 units was administered intravenously. The activated clotting time (ACT) was maintained at 350–400 seconds. Nitroglycerin was given prior to the procedure and during the procedure by intracoronary injection, intravenously, or topically at the discretion of the investigator. Reopro was not utilized in this study. After completion of the procedure, patients were treated with overnight infusion of heparin after which time the vascular sheaths were removed.

Definitions

For the purpose of this study, *laser success* was defined as a decrease in diameter stenosis ≥20% after laser application, and *procedural success* was defined as a final reduction of lumen stenosis <50% (after laser alone or after laser and adjunctive percutaneous transluminal coronary angioplasty [PTCA]) in the absence of a major complication (death, emergency bypass surgery, or Q-wave myocardial infarction). Failure was defined as inability to achieve <50% residual stenosis or the occurrence of a major complication. Dissection was defined by the classification of Huber et al. [6]. Dissection was considered to be major if it was associated with death, myocardial infarction, or the need for bypass surgery, and was considered minor if it led to no clinical complication. Acute closure was defined as reduced antegrade flow (TIMI ≤1) caused by acute occlusion of the target lesion. Q-wave infarction was diagnosed as elevation of creatine kinase above laboratory normal values with any MB fraction and the development of Q-waves on electrocardiogram (EKG). Non-Q wave infarction was defined as persistent ST-segment or T-wave changes on the post-procedural EKG with CK determination of ≥1.5 times normal with a positive myocardial band. Unstable angina was defined by new-onset angina, rest angina, or crescendo angina within 6 weeks. Intracoronary thrombus formation was defined as development of an intraluminal lucency, filling defect, or straining consistent with angiographic appearance of a thrombus: Perforation was defined as persistent extravascular collection of contrast medium beyond the vessel wall with or without associated clinical complications [7]. Coronary spasm was defined as transient diminution of blood flow with reduction in vessel caliber

relieved either spontaneously or by nitroglycerin administration. Groin site complication required blood transfusion or surgical intervention.

Angiographic Assessment

All angiograms were initially categorized by lesion location and evaluated by individual operators utilizing digital calipers or visual assessment for lesion severity, expressed as percent of lumen diameter. American College of Cardiology/American Heart Association criteria for type A, B, and C lesion classification were applied [8]. In follow-up angiograms, restenosis was defined as >50% lumen diameter stenosis at the site of laser angioplasty. Quantitative coronary arteriography on 105 cine films was performed at an independent core laboratory at Stanford University (Palo Alto, CA), which was blind to the clinical data and outcome of the procedure.

Statistical Analysis

Data are reported using percentages for categorical variables and mean ± standard deviation for continuous variables. Logistic multiple stepwise regression models were used to explain the individual and joint relationships between lesion and baseline characteristic data and the outcomes of laser success and procedural success. Complication rates were reported using percentages and 95% confidence intervals. Univariate and multivariate analysis were done to predict various complications using logistic regression models. Odds ratios (OR) were calculated to give the likelihood that patients with a given variable had increased or decreased likelihood of an outcome, as compared with all other patients without the variable. The pre-laser, post-laser, and final stenoses were compared using repeated measures analysis of variance. Individual comparisons of stenosis were done using a pairwise t-test for correlated data with a family-wise significance of 0.0166. All other tests considered a P value of <.05 significant. Statistical analyses were performed with a standard package at Duke Clinical Research Institute, Duke University (Durham, NC).

RESULTS

Baseline

Mid-infrared laser-assisted angioplasty was performed on 2,038 lesions in 1,862 consecutive patients with a mean age of 61 ± 11 years (75% men) [Table 1]. Clinical indications for laser-assisted angioplasty included unstable angina (69%), stable angina (20%), positive exercise test (5%), and acute myocardial infarction (6%). Prior angioplasty had been performed in 30% of lesions.

TABLE 1. Holmium Laser Multicenter Registry

No. of patients	1,862
No. of lesions	2,038
Pts age	61 ± 11
Males	75%
Pt Hx	
Myocardial infarction	44%
Congestive heart failure	9%
Diabetes	21%
Hypertension	54%
Smoking	49%
Hypercholesterolemia	57%
Prior angioplasty	30%
Prior bypass surgery	17%
Indications for procedure	
Positive Exercise Test	93 (5%)
Stable Angina	372 (20%)
Unstable Angina	1,285 (69%)
Acute myocardial infarction	112 (6%)
ACC/AHA lesion classification	
A	245 (12%)
B1	387 (19%)
B2	856 (42%)
C	550 (27%)
Lesion location	
Left anterior descending	815 (40%)
Right coronary artery	649 (32%)
Circumflex artery	358 (17%)
Saphenous vein graft	216 (11%)

Coronary artery disease (diameter stenosis >50%) involved one vessel in 46% of patients, two vessels in 23% of patients, and three vessels in 31% of patients. Complex morphology (ACC/AHA B_2 plus C types) was identified in 68.4%. The mean lesion length was 13 ± 11 mm; 108 ± 113 laser pulses were emitted per lesion. Baseline lesion characteristics are described in Tables 1 and 2.

Immediate Results

Pre-laser stenosis was reduced from 90 ± 10% to 64 ± 21% by the laser irradiation. A mean of 108 ± 113 pulses were delivered to the lesions. Adjunct balloon angioplasty achieved a 21 ± 19% final residual stenosis. Figure 1 depicts cumulative distribution of values for percent stenosis.

The final laser catheter tip size was 1.2 mm in 388 lesions (29.6%), 1.3 mm in 160 lesions (12.2%), 1.4 mm in 242 lesions (18.5%), 1.5 mm in 360 lesions (27.5%), 1.7 mm in 107 lesions (8.2%), and 2.0 mm in 52 lesions (4.0%). The mean laser catheter tip diameter was 1.40 ± 0.19 mm. The

TABLE 2. Baseline Lesion Characteristics

Variable	Total No. of documented lesions	Incidence (%)
Length	1,812	
<10		735 (40.6)
10–20		821 (45.3)
>20		256 (14.1)
Tortuosity	1,229	
No		919 (74.8)
Moderate		279 (22.7)
Severe		31 (2.5)
Angulation	1,226	
<45		1,090 (88.9)
45–90		129 (10.5)
>90		7 (0.6)
Eccentric	1,257	61.7%
Contour (irregular)	1,180	57.9%
Calcium	534	26.2%
Ostial	224	11.0%
Bifurcation	67	3.3%
Thrombus-prelaser	611	30.0%
Graft	216	10.6%
Total occlusion	279	13.7%

average vessel diameter was 3.36 ± 2.85 mm and thus the average catheter tip diameter/vessel diameter ratio was 0.41 ± 0.11, consistent with the practice of sizing the laser catheter to match the stenosis severity rather than matching normal vessel reference diameter. Laser success was achieved in 1620 (87.3%, [95% CI: 85.8–88.8]) of the patients and final procedural success was achieved in 93% patients (95% CI: 92.0–94.25%). In the subgroup of 105 patients with quantitative coronary arteriography the minimal luminal diameter increased from 0.8 ± 0.5 mm (mean ± SD) to 1.3 ± 0.5 mm after laser ablation ($P < .001$) and to 1.9 ± 0.5 mm following adjunct balloon angioplasty ($P < .001$). The mean percent diameter stenosis was reduced from 77 ± 16% (mean ± SD) to 56 ± 14% after laser treatment ($P < .001$) and was further decreased by balloon angioplasty to 37 ± 13% ($P < .001$).

Predictors of Laser and Procedural Success

A multivariable stepwise logistic regression model was used to predict the effect of lesion morphology on procedural outcome identifying bifurcation lesion (76.2%, OR = 0.5 [95% confidence interval 0.2, 1.0], $P = .05$) and severe tortuosity of the treated vessel (71.0%, OR = 0.4 [95% confidence interval 0.2, 0.9], $P = .02$) as significant multivariable predictors of decreased laser success. The relation between lesion type (by modified ACC/AHA classification) and early laser angioplasty outcome is shown in Table 3. Procedural success was achieved in 94%, 94%, 93%, and 93% of type A, B_1, B_2, and C lesions, respectively (P = ns). Significantly more laser energy was needed to achieve successful recanalization of total occlusions as compared with nontotal occlusions (138 ± 20 vs. 103 ± 113 pulses [$P < .001$], respectively). However, final success rate was similar (94% vs. 92%, P = ns) in these two groups. More energy was needed for calcified stenoses versus noncalcified lesions (119 ± 91 vs. 101 ± 86, respectively, $P = .0002$), and success, although high, was significantly less than in noncalcified lesions (90% vs. 95%, $P < .001$, respectively). When only lesion morphologic variables were considered in the multivariate analysis (Fig. 2) the presence of thrombus within the target lesion was a predictor of procedural success (OR = 2.0 [95% confidence interval 1.0–4.0], $P = .04$), while calcium within the lesion was associated with reduced procedural success (OR = 0.6 [95% confidence interval 0.3–1.0], $P = .04$).

Effect of Lesion Location

Table 4 depicts success rate and incidence of abrupt closure according to target vessel. Successful final results were obtained in 1,905 (93%) of lesions. There was no significant difference between lesions located in either epicardial coronary arteries or saphenous vein grafts. The incidence of acute closure varied from 1.4% in saphenous vein grafts and circumflex artery to 2.5% in the right coronary artery and 3.1% in left anterior descending artery; however, statistically, there was no difference between the vessels treated.

Complications

There were 71 major complications in 1,862 procedures (3.8%); [95% confidence interval: 2.9% to 4.7%] (Table 5). Four of the 14 deaths occurred as a result of complex dissection, four were attributed to acute closure, one to localized perforation leading to vessel closure, one due to perforation causing tamponade, one to distal embolization causing non-Q-wave myocardial infarction, one to pulmonary edema subsequently leading to emergency coronary artery bypass surgery, one to preexisting thrombosis leading to non-Q-wave infarction, and one due to loss of distal side-branch caused by adjunct directional atherectomy leading to acute infarction. The 23 Q-wave-myocardial infarctions were due to major dissection in 13 cases, severe coronary spasm in three cases, abrupt closure in two cases, thrombosis in two patients, and to an unknown cause in three pa-

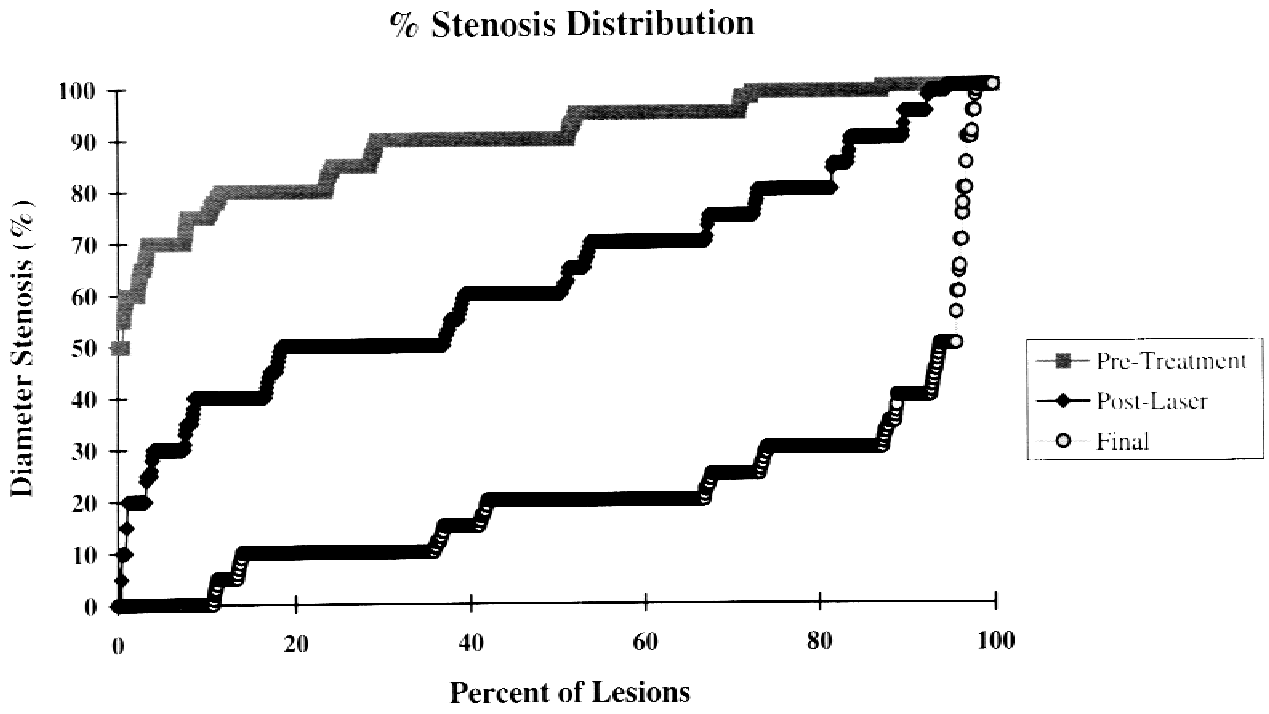

Fig. 1. Cumulative distribution of values for percent stenosis. Compared with the pre-procedural values (pretreatment), the improvement after holmium: YAG laser treatment (post-laser) and after adjunct balloon dilation are shown for percent stenosis.

TABLE 3. Technical Data for 1905 Lesions*

Lesion	Pre-proc %	Post-laser %	Final %	No. of pulses	Success rate %
Type					
A	86 ± 10	60 ± 20	19 ± 11	85 ± 59	94
B1	87 ± 10	58 ± 22	18 ± 11	118 ± 191	94
B2	91 ± 10	64 ± 20	18 ± 12	93 ± 73	93
C	92 ± 10	65 ± 20	18 ± 12	131 ± 106	93
P value	A-B2, A-C, B1-B2, B1-C: <001 B2-C: .02	A-B2: .007 A-C: .003 B1-B2, B1-C: <001	NS	A-B1: .022 A-C, B2-C: <001 B1-B2: .02	NS
Total occlusion					
Yes	100 ± 0	73 ± 20	18 ± 13	138 ± 120	94
No	88 ± 10	61 ± 20	19 ± 12	103 ± 13	92
P value	<.001	<.001	NS	<.001	NS
Calcified					
Yes	89 ± 10	64 ± 20	20 ± 12	119 ± 91	90
No	90 ± 10	62 ± 20	18 ± 12	101 ± 86	95
P value	NS	NS	0.01	0.0002	<0.001
Total	90 ± 10	62 ± 21	18 ± 12	107 ± 114	

*Data presented are mean ± SD.

tients. Seven of these Q-wave myocardial infarctions were a complication of an emergency coronary artery bypass surgery. Perforations occurred in 40 cases, leading to further adverse events in 17 patients including the following: death in three patients, emergency bypass surgery in nine patients, non–Q-wave infarction in four patients, and acute closure in one patient. Severe spasm leading to myocardial infarction occurred in 19 (8% of those with spasm) of patients. Less severe spasm occurred in 215 patients and was treated with repeat balloon inflations and with intracoronary nitrates.

Multivariable stepwise logistic regression analysis (Fig. 3) did not identify any significant predictor of major complications as a group

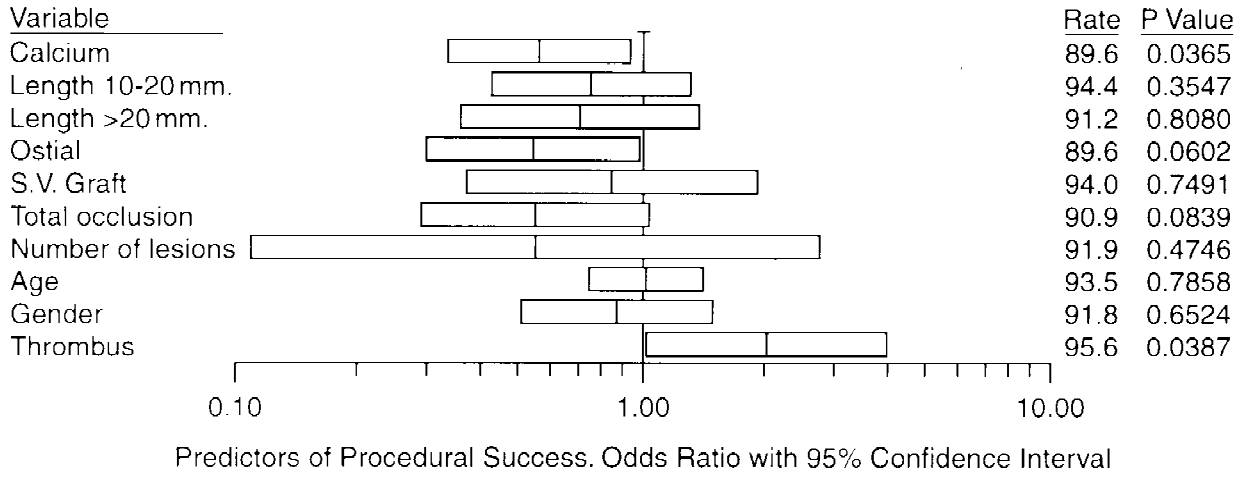

Fig. 2. Predictors of procedural success. The likelihood of procedural success for a series of variables is given by the raw success rates, odds ratio, and *P* values obtained by multivariable logistic regression analysis. The statistical reliability of the odds ratio is given by the 95% confidence interval. Variables with an odds ratio significantly >1.0 are associated with increased likelihood of success. Rates for variables are grouped as female for gender, age >65 years for age, and number of lesions >1 for number of lesions.

TABLE 4. Laser-Assisted Angioplasty Success and Abrupt Closure According to Lesion Location

Lesion location	No. of target lesions	Success (%)	Abrupt closure (%)
LAD	815	760 (93)	25 (3.1)
RCA	649	597 (92)	16 (2.5)
Cx	358	345 (96)	5 (1.4)
SVG	216	203 (94)	3 (1.4)
P value		NS	NS
Total	2,038	1,905 (93)	49 (2.4)

(death, Q-wave MI, and emergency CABGs). Table 6 depicts univariable and multivariable analysis of factors associated with individual complications (with the exception that univariable and multivariable models were not done to predict death or Q-wave infarction individually due to the small number of events). There were no significant factors associated with acute closure. Total occlusion was associated with the need for emergency coronary bypass surgery. The presence of an ostial lesion, a lesion within a saphenous vein graft, and the number of lesions were significantly associated with non–Q-wave myocardial infarction. Overall, non–Q-wave myocardial infarction was more likely to occur in patients with ostial lesion (5.7% vs. 3.0% for nonostial lesion, $P = .04$), with two or more lesions (6.4% vs. 3.2% for one lesion, $P = .05$) and with target lesion within a saphenous graft (7.6% vs. 2.9% for coronary lesion, $P = .0007$). Factors associated significantly with dissections (minor and major combined) were the lesion's length, ostial location, a saphenous vein graft, bifurcation, tortuosity, angulation, gender, and prior CABGS.

Follow-Up

Complete clinical follow-up was available in 1,206 (74%) of 1,625 eligible patients at an interval of 6.5 ± 1.5 months after discharge. At 6 months follow-up, anginal symptoms were reported as improved in 741 patients (71%), unchanged in 135 patients (13%), and worse in 164 patients (16%) as compared with anginal symptoms immediately before laser angioplasty. Late cardiac outcomes included recurrent angina in 234 patients (19.7%), repeat percutaneous intervention on the original target lesion (either balloon angioplasty or another device) in 213 patients (17.7%), coronary artery bypass surgery in 140 patients (11.6%), Q-wave myocardial infarction in 13 patients (1.1%), non–Q-wave infarction in 15 patients (1.2%), and late cardiac death in 21 patients (1.7%). Therefore, clinical restenosis occurred in 636 patients (34%). Angiographic evaluation was available in 797 (54%) of 1,484 eligible lesions. With a restenosis definition of a diameter stenosis ≥50%, 434 lesions (54%) had angiographic evidence for restenosis, including 102 lesions (13%) exhibiting total occlusion of the original target lesion.

DISCUSSION

Mid-Infrared Laser–Thrombus Interaction

The presence of coronary thrombus has been associated with complications during and after

TABLE 5. Incidence of Complications During 1,862 Procedures

	No. of complications	% of procedures	95% confidence interval
Major complications	83	3.8	2.9–4.7
Death	14	0.8	0.4–1.1
Emergency CABGS	46	2.5	1.8–3.2
Q-wave infarction	23	1.2	0.7–1.7
Other complications			
Acute closure	47	2.5	1.8–3.2
Perforation	40	2.2	1.5–2.8
Dissection			
Total	322	17.3	15.6–19.0
Major	109	5.8	7.1–15.7
Minor	213	11.4	1.4–10.2
Non–Q-wave infarction	64	3.4	2.6–4.3
Spasm	234	12.6	11.1–14.1
Thrombosis	46	2.5	1.8–3.2
Embolization	26	1.4	0.9–1.9
Loss of side-branch	25	1.3	0.8–1.8
Groin complication	8	0.4	0.1–0.7

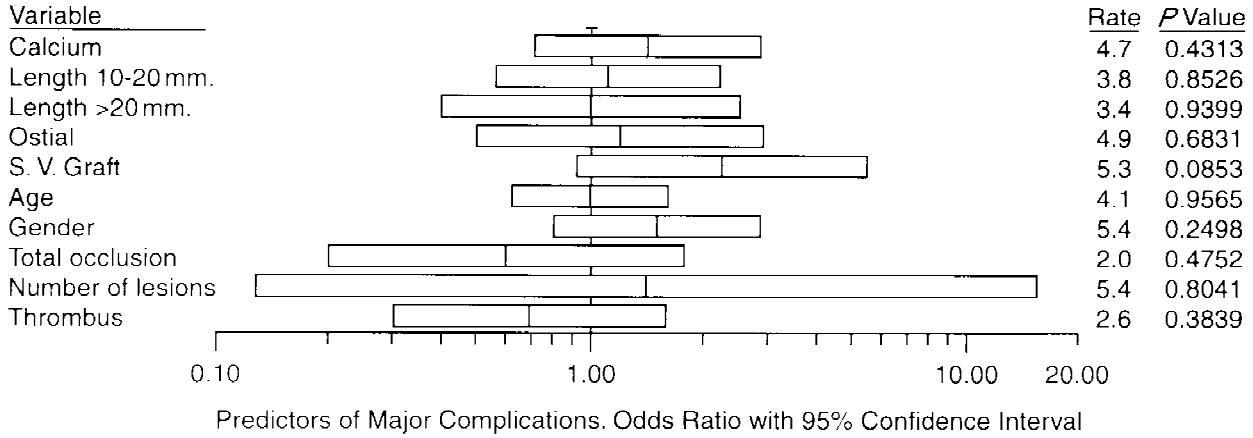

Fig. 3. Predictors of major complications (death, emergency CABGS, and Q-wave myocardial infarction). The likelihood of complications for a series of variables is given by the raw complication rates, odds ratio, and *P* values obtained by multivariable logistic regression analysis. The statistical reliability of the odds ratios is given by the 95% confidence interval. Rates for variables are grouped as female for gender, age >65 years for age, and number of lesions >1 for number of lesions.

coronary angioplasty [9]. Thrombi are known to have a high water content, resulting in a large thermal sink and dissipation of laser energy [10]. As thrombi avidly absorb light in the mid-infrared optical range [11], the mid-infrared holmium: YAG laser potentially offers a unique revascularization option for patients with thrombotic occlusions [12]. In a recent in vitro study we determined this laser clot-dissolving by a mechanical, nonselective process caused by the formation and propagation of shock waves [13]. The induction and radial distribution of a shock-wave front creates local tissue fragmentation with subsequent lysis. In the present clinical study the presence of angiographically detected thrombus was a predictor of procedural success. In contrast, Estella and colleagues have shown that success of excimer laser is significantly compromised when thrombus is treated [14]. This difference between ultraviolet and mid-infrared laser may be attributed to the shallow penetration depth of the excimer beam (30–50 μm) as compared to that of the holmium (400–500 μm). The excimer's shallow in-plaque penetration necessitates direct contact with the thrombotic plaque, leading to trauma and embolization. The mid-infrared laser has been successful in the treatment of thrombotic lesions [15–18], and especially in patients sustaining acute myocardial infarction who present with large thrombus burden resistant to thrombolytic drugs [19–21]. Nevertheless, despite the potential advantages and reported clinical success of this laser,

TABLE 6. Univariable and Multivariable Analysis of Factors Associated With Complications in 1,862 Procedures

Complication	Univariate analysis	Multivariate analysis
Emergency CABGS	Total occlusion	Total occlusion
Non–Q-wave MI	Ostial; graft; number of lesions	Graft, number of lesions
Dissection	Calcium; ostial; graft; lesion's length; bifurcation; gender; prior CABGS; tortuosity; angulation	Lesion's length, graft, gender
Acute closure	No significant predictors	No significant predictors

other less expensive percutaneous devices or pharmacologic agents can, as well, achieve success in these lesions. Among these modalities are balloons [22], ultrasound [23], and glycogen IIb/IIIa receptor antagonists [24] and coronary stents [25]. Randomized studies will be required to prove cost-effectiveness of laser catheter for thrombus in acute myocardial infarction and unstable angina.

Safety and Complications

The complexity of target occlusions in this study is reflected in the baseline lesion characteristics, which include lesion type B2 (41.3%) and C (27.1%), saphenous vein grafts (10.8%), thrombus (30%), and calcification (26.2%). These lesions are non-ideal for balloon angioplasty, yielding relatively low success and high complication rates [26,27]. The overall incidence of complications with the mid-infrared laser in these lesion subtypes compares favorably to other debulking devices such as rotational atherectomy [28], directional atherectomy [29], and excimer laser [2,3].

During pulsed-wave laser emission powerful acoustic compression is generated within the laser plaque [30]. Clinically, these acoustic waves can cause dissections and perforations [31]. Furthermore, any laser—whether excimer or holmium—generates vapor gas bubbles during plaque ablation. The relatively high rate of dissections accompanying laser irradiation is attributed to the rapid expansion and implosion of the vapor bubbles [32]. Acute closure during lasing is attributed to formation of multilayered wall dissections that occlude the arterial lumen, a phenomenon termed the "mille feuilles" effect [33]. Among the most common causes of laser-induced coronary perforations are forced lasing, using unrecommended fluences, attempting multiple passes through an already dissected lesion, oversizing of catheter and breaching of recommended indications [34]. From the experience of the excimer laser investigators [35], as well as from the present experience, many perforations can be managed locally, and over time, with increasing operator experience, the frequency of coronary artery perforation significantly declines [15,35].

With appropriate case selection and with application of careful lasing techniques [5], mid-infrared laser-induced complications such as perforation, major dissections, acute closure, embolization, and spasm may be significantly reduced [15].

Plaque Characteristics and Laser Energy

Calcified lesions required significantly more energy for ablation, and the success rates are significantly less than in non-calcified lesions. This corroborates previous observations by Bonner et al. [36] who found that although calcified tissue may be ablated by mid-infrared laser in wet-field ablation of calcified atheroma, efficiency is low and threshold fluences are high.

De novo lesions contain fibrosis, cholesterol-rich plaques, and frequently thrombi, whereas restenotic lesions are largely composed of smooth muscle cell proliferation. In a previous report on the first 1,340 patients of the multicenter study, we compared de novo lesions with restenotic lesions [37]. Restenosis lesions required significantly more mid-infrared laser energy to achieve recanalization than de novo plaques (130 ± 123 vs. 109 ± 81 pulses, $P = .001$). Yet, laser success rates were similar in both types of lesions (86% vs. 87%, respectively, P = ns), as well as rates of death, emergency bypass operation, and non–Q-wave myocardial infarction. However, Q-wave myocardial infarction was higher in de novo lesions than in the restenosis lesions (1.4% vs. 0.2%, $P = .05$), presumably due to the frequent presence of thrombi within the de novo plaques. The angiographic restenosis rate was similar in both groups (45% in restenosis vs. 49% in de novo lesions, P = ns). Thus, the composition of the target plaque appears to affect energy level required and the incidence of procedural related Q-wave myocardial infarction.

Role of Adjunctive Balloon Angioplasty After Laser Angioplasty

Device success was achieved in 87% of lesions, and 40% of lesions had residual stenosis ≤50% after laser angioplasty (Fig. 1). Because sizing of the laser catheter is tailored to lesion severity, in most cases catheter diameter was <2.0 mm, leading to the use of adjunctive balloon dilatation, which was necessary in almost all cases to ensure adequate final lumen dimension. This situation proves that the idea of "laser stand alone" is unrealistic. The need to apply balloon adjunctly to laser treatment has an effect on the overall cost of the procedure and therefore mandates a careful selection of lesions for this procedure, i.e., only complex lesions which indeed are non-ideal for balloon angioplasty and cannot be successfully treated by an alternate, less expensive percutaneous debulking device.

Restenosis

Laser angioplasty was introduced with the hope of reducing both the frequency of complications associated with balloon angioplasty and a restenosis rate as high as 50–60%. Using the conventional dichotomous definition of restenosis, the 6-month angiographic restenosis after mid-infrared laser assisted angioplasty was 54%, as compared to 46% restenosis rates for excimer laser angioplasty [31], 57% restenosis rates reported for balloon angioplasty [38], 50% for directional atherectomy [38], 38% for rotational atherectomy [28], and 14% for stents [39]. Thus, this study corroborates the suggestion that lasers, regardless of wavelength, do not significantly reduce restenosis rates [40].

Limitations of the Study

This is a nonrandomized, observational study, and as such, was not designed to explore the best percutaneous treatment for patients with significant coronary artery disease. Thus, definite recommendation on the use of holmium laser cannot be made with any certainty. Quantitative coronary arteriography in an independent core laboratory has been done in only 105 patients. Had it been done in all patients, it could have eliminated known inherited biases of investigators, such as underestimation of the final diameter stenosis, and potentially, other predictors of success and complications may have been identified. Nevertheless, quantitative coronary arteriography was also not performed in other debulking device registries with similar safety and efficacy data [2,28]. Another weakness of this study was the 54% 6-month angiographic follow-up rate. This relatively low rate is a result of the manufacturer's decline to sponsor repeat angiograms and the refusal of insurance companies to pay for repeat catheterizations for asymptomatic patients. In the future, the FDA may have to seek ways to ensure that repeat angiography and complete clinical follow-up will be performed.

CONCLUSIONS

Elective use of mid-infrared coronary laser angioplasty is associated with high immediate success rates and acceptable major complication rates. The presence of a thrombus within the target lesion is a predictor of procedural success, while the presence of calcium reduces the success rate. Notably, restenosis rates are above 50%, therefore reserving this expensive technology for selective patients with selective complex lesions. Thrombotic lesions which fail to respond to thrombolytic agent and cannot be treated by a less expensive percutaneous device may be a suitable target. Randomized trials are required to clearly prove whether this device offers any real clinical advantages over stand-alone balloon angioplasty, while being cost-effective.

ACKNOWLEDGMENTS

The authors appreciate the invaluable assistance of Laurie Topaz and Michelle Martin in the preparation of this manuscript.

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APPENDIX

The Holmium Multicenter Study: participating centers contributing data for this report and corresponding clinical investigators:

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Audubon Regional Medical Center, Louisville, KY, Richard Allen, David Dagerforde

University Hospital, Augusta, GA, Paul Cundey, Ray Johnson, John Kelly

Baptist Hospital, Little Rock, AR, Randal Hundley, James Shuffield

Baystate Medical Center, Springfield, MA, John Joelson, Alan Wiseman

Blodgett Memorial Medical Center, Grand Rapids, MI, Ray Roden, Ronald Vanderlaan

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Community Hospital of Indianapolis, Indianapolis, IN, Edward Harlamert, Don Ziperman

Cooper Hospital, Camden, NJ, William Groh, Peter Kurnik

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Episcopal Hospital, Philadelphia, PA, Vidya Banka

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University Medical Center, Tucson, AZ, Samuel Butman

West Virginia, Morgantown, VA, Abnash Jain

Westchester Hospital, Westchester, NY, Martin Cohen, Melvin Weiss